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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,982	01/10/2001	Susan Acton	MP198-052P1RDV10M	1338

7590 07/02/2003

MILLENNIUM PHARMACEUTICALS, INC.
INTELLECTUAL PROPERTY GROUP
75 SIDNEY STREET
CAMBRIDGE, MA 02139

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,982	ACTON, SUSAN	
	Examin r	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 27-40 are pending and currently under examination.

2. Applicant's election without traverse of claims 27-40 drawn to an antibody or portion thereof that specifically binds to a polypeptide comprising amino acid sequence of SEQ ID NO:5 (CSAPK-2)or a fragment thereof filed on 4/17/02, is acknowledged.

3. The specification on page 1 should be amended to reflect the status of parent application No. 9/163,115.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Non-initialed and non-dated alterations of the residence have been made to the oath or declaration by Susan Acton. See 37 CFR 1.52(c).

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

In addition, Applicant should avoid the use of novel in the title, as patents are presumed to be novel and unobvious.

6. Claims 38 and 39 are objected to because of the following informalities: the function word that indicate the derivation of amino acid residues should be "of" rather than "or". Appropriate correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed. *This is a New Matter rejection*:

The phrase "human antibody" claimed in claim 36, line 2 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 4-17-03 points to the specification at pages 37-39 for support for the newly added limitations "human antibody" as claimed in claim 36. However, the specification does not provide a clear support of "human antibody". The instant claim now recites a limitation, which was not clearly disclosed in the specification and claims as originally filed.

7. Claims 27-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or portion thereof that specifically binds to SEQ ID NO:5, and amino acid 31-277 and 407-421 fragments for diagnostic test, does not reasonably provide enablement for an isolated antibody, or potion thereof, that specifically binds to (a) any polypeptide "comprising" the amino acid sequence set forth in SEQ ID NO:5 or any "fragment thereof" in claim 27, (b) any polypeptide encoded by the nucleic acid molecule "comprising" the nucleotide sequence of SEQ ID NO:4 or 6, or any "fragment thereof" in claim 28, (c) any polypeptide encoded by a nucleic acid molecule comprising the nucleotide sequence contained in the plasmid deposited with the ATCC as Accession Number 203306 or any "fragment thereof" in claim 29, wherein the said antibody binds to any "fragment of said polypeptide "comprising" amino acid residues 31-277 of SEQ ID NO: 5 in claim 38, wherein said antibody binds to any "fragment" of said polypeptide "comprising" amino acid residues 407-421 of SEQ ID NO:5 in claim 39. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use antibodies, wherein the antibodies binds any polypeptide fragment of SEQ ID NO:5, encoded by any fragment of SEQ ID NO: 4 or 6; or any fragment of the plasmid deposited with the ATCC as Accession number 203306.

Claims 27-29 and 38-39 require antibody to bind to different polypeptides. However, the present specification fails to provide sufficient disclosure of amino acid fragments that maintain the structural and functional properties of the CSAPK-2 activity set forth in SEQ ID NO:5, wherein the fragment is immunogenic. The specification does not provide sufficient guidance as to which of the amino acids may be changed while CSAPK-2 functional activity is retained. In addition, the term "comprising" in claims 27-29 and 38-39 is open-ended, it expand the fragment of the amino acid sequence of SEQ ID NO: 5", the "31-277 fragment", the "407-421" and the "encoded fragment of the nucleic acid sequence of SEQ ID NO:4 or 6" to include additional non disclosed amino acids. Further, the team "comprising" would expand the nucleic acid fragment of SEQ ID NO:4, 6, or the one derived from the plasmid to contain additional non recited nucleic acid.

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary

structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al*., (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at the claimed fragments having CSAPK-2 activity.

The scope of the claimed antibodies that is specifically binds to SEQ ID NO:5 is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of amino acid sequences broadly encompassed by the claimed invention as recited in claims 27-29 and 38-39. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a peptide's amino acid sequence, and, in turn, nucleic acid sequence and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the peptide's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 27-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody or portion thereof that specifically binds to SEQ ID NO:5, and amino acid 31-277 and 407-421 fragments for diagnostic test.

Applicant is not in possession of an isolated antibody, or potion thereof, that specifically binds to (a) any polypeptide "comprising" the amino acid sequence set forth in SEQ ID NO:5 or any "fragment thereof" in claim 27, (b) any polypeptide encoded by the nucleic acid molecule "comprising" the nucleotide sequence of SEQ ID NO:4 or 6, or any "fragment thereof" in claim 28, (c) any polypeptide encoded by a nucleic acid molecule "comprising" the nucleotide sequence contained in the plasmid deposited with the ATCC as Accession Number 203306 or any "fragment thereof" in claim 29, wherein the said antibody binds to any "fragment of said

polypeptide "comprising" amino acid residues 31-277 of SEQ ID NO: 5 in claim 38, wherein said antibody binds to any "fragment" of said polypeptide "comprising" amino acid residues 407-421 of SEQ ID NO:5 in claim 39.

Applicant has disclosed only amino acid of SEQ ID NO: 5 encoded by SEQ ID NOs: 4 and 6; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
June 30, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600